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Clinical and Molecular Epidemiology of *Histoplasma capsulatum* in Quebec, Canada

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Background

Histoplasma capsulatum comprises eight phylogenetically distinct clades as defined by multilocus sequence typing (MLST). Limited animal data suggest that virulence of North American and Latin American strains of *H. capsulatum* may differ, hypothetically accounting for unique clinical features observed in cohorts from different locations. Differential clinical disease has never been studied in patients with genotype-defined histoplasmosis.

Methods

We conducted a retrospective cohort study including all culture-proven histoplasmosis cases from four university-affiliated hospitals in Quebec (Canada), between 1988-2013. *H. capsulatum* isolates were genotyped using MLST. Demographic and clinical data were independently collected by chart review.

Objectives

The present study aimed to :

1. Define the clinical differences between patients infected by phylogenetically distinct clades of *H. capsulatum*
2. Obtain a better understanding of the epidemiology of *H. capsulatum* in Quebec, Canada through MLST

Results

Table 1. Demographics and clinical data for all patients and according to *H. capsulatum* genotype

	All patients n = 72	NAm2 n = 37	LAmA n = 28	Others n = 7
Age (Y), mean ± SD	46,3 ± 14,8	**50,1 ± 14,0**	**41,6 ± 15,6**	45,3 ± 11,5
Male sex	73,6	78,4	75,0	42,9
Caucasian	77,8	100,0	67,9	0,0
Latino-American	9,7	0,0	17,9	28,6
Other ethnicity	12,5	0,0	14,3	71,4
Born in Quebec	68,1	86,5	60,7	0,0
Diabetes	11,1	13,5	3,6	28,6
COPD	13,9	**24,3**	**3,6**	0,0
Immunosuppression				
Any	73,6	64,9	82,1	85,7
HIV	41,7	**18,9**	**64,3**	71,4
Malignant hemopathy	4,2	5,4	3,6	0,0
SOT	11,1	18,9	3,6	0,0
Rheumatologic disease	8,3	8,1	10,7	0,0
Other	8,3	13,5	0,0	14,3
Clinical syndrome				
PDH	59,7	**43,2**	**71,4**	100,0
Acute PH	22,2	27,0	21,4	0,0
Chronic PH	8,3	13,5	3,6	0,0
Other	9,7	16,2	3,6	0,0
Disease severity				
Hospital stay (D), mean ± SD	32,8 ± 35,9	36,2 ± 45,9	30,0 ± 24,2	28,8 ± 16,5
Use of amphotericin B	51,4	40,5	64,3	57,1
Admission to ICU, intubation and/or death	19,4	16,2	25,0	14,3

NB : Bold variates demonstrated a statistically significant difference ($p < 0,05$; Fisher's exact test) between NAm2 and LAmA genotypes. All data shown as percentage unless specified otherwise. SD : standard deviation, COPD : chronic obstructive pulmonary disease, HIV : human immunodeficiency virus, SOT : solid organ transplantation, PH : pulmonary histoplasmosis, PDH : progressive disseminated histoplasmosis, ICU : intensive care unit.

Results

Figure 1. Maximum parsimony phylogenetic tree of clinical strains of *H. capsulatum* and their relative frequencies

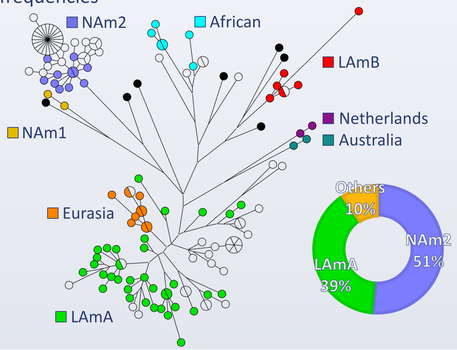


Figure 2. Immunosuppression, according to *H. capsulatum* genotype

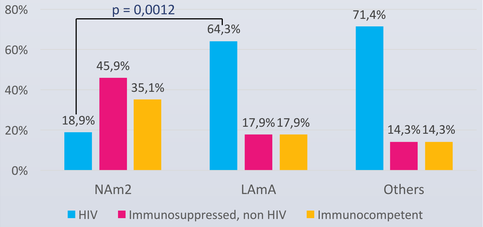
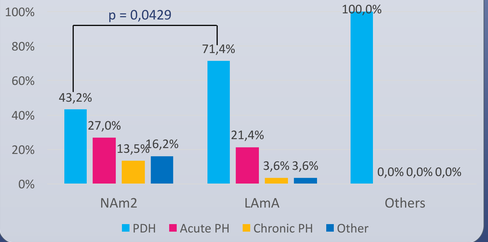


Figure 3. Clinical syndrome, according to *H. capsulatum* genotype



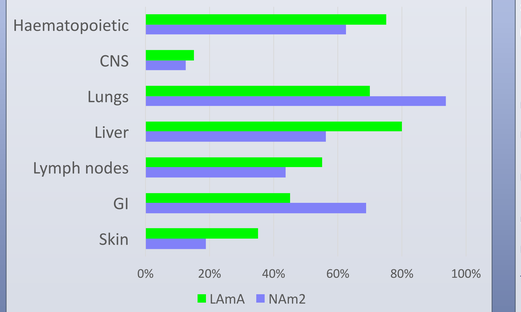
Subgroup analyses

Progressive Disseminated Histoplasmosis

Table 2. Demographics and clinical outcome of patients affected by PDH, according to genotype

	NAm2 n = 16	LAmA n = 20	p-value
Age (Y), mean ± SD	**51,9 ± 15,3**	**40,8 ± 12,9**	**0,0237**
Male sex	93,8	85,0	0,6129
HIV infection	**37,5**	**75**	**0,0409**
Clinical outcome			
Hospital stay (D), mean ± SD	**58,9 ± 58,2**	**28,9 ± 17,3**	**0,0356**
Use of amphotericin B	68,8	70,0	1,0000
Admission to ICU, intubation and/or death	37,5	30,0	0,7295

Figure 4. Organ systems affected in progressive disseminated histoplasmosis, according to genotype



Caucasian patients

Table 3. Clinical data of Caucasian patients, by genotype

	NAm2 n = 37	LAmA n = 19
Age (Y), mean ± SD	50,1 ± 14,0	43,2 ± 17,6
Male sex	78,4	84,2
HIV infection	**18,9**	**52,6**
Recent travel history	**2,7**	**47,4**
Progressive disseminated histoplasmosis	43,2	63,2
PDH : skin manifestations	18,8	25,0
Use of amphotericin B	40,5	52,6
Admission to ICU, intubation or death	18,9	15,8

Conclusions

Patients with LAmA histoplasmosis were more likely to have PDH as compared with NAm2-infected patients.

- The association was not significant within Caucasian patients, suggesting that host susceptibility may be at play, although power was limited in this subgroup analysis.
- Patients with LAmA were also more likely to be co-infected with HIV, which may be a confounder.
- Multivariate analysis will be performed to assess whether LAmA is an independent predictor of PDH

We did not confirm distinct clinical features between NAm2 and LAmA histoplasmosis, although the study was under-powered to detect small differences.

In our endemic region, a significant proportion of culture-proven histoplasmosis was not indigenous (travel- or immigration-associated).

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